REMARKS

The Official Action of February 25, 2004 has been carefully considered and reconsideration of the application as amended is respectfully requested.

Claim 14 has been canceled because it did not properly depend from claim 11, which recites that the patient has a disease selected from chronic hepatitis C and cirrhosis caused by hepatitis C virus. Claim 14, on the other hand, recited that the disease is hepatocellular carcinoma.

Claims 11-14, 16-22 and 23-27 stand rejected under 35 USC 103(a) as allegedly being unpatentable over Foster et al in view of Albrecht. Applicants respectfully traverse these rejections.

The claimed invention is based upon Applicants' discovery that, when a patient is infected by hepatitis C virus, there is a marked reduction in the expression of a specific IFN-alpha subtype, namely IFN-alpha 5. This led Applicants to the realization that a patient with hepatitis C virus could be treated by raising the level of IFN-alpha 5 in the patient. With Applicants' Amendment dated October 21, 2003, Applicants submitted a Declaration under 37 CFR 1.132 authenticating the results of experimentation which shows that IFN-alpha 5 induces stronger activation signals and higher expression of antiviral genes in hepatocytic cells than the subtype currently used in antiviral therapy of chronic viral hepatitis, IFN-alpha 2. (An originally signed

declaration is submitted herewith to replace the copy submitted previously.)

As acknowledged by the Examiner in the second paragraph on page 4 of the Official Action, the primary reference, Foster et al, does not teach specific virus such as HCV causing diseases related to the liver or recite the diseases. It also does not teach the use of IFN-alpha in patients having chronic hepatitis C infection. It *a fortiori* does not teach the use of the claimed subtype, IFN-alpha 5, in patients having chronic hepatitis C infection.

The Examiner attempts to remedy the deficiency in the primary reference by citing Albrecht, which allegedly teaches the use of IFN-alpha in patients having chronic hepatitis C infection to radicate HCV. However, even assuming for the sake of argument that this were true, Albrecht could not be properly combined with Foster et al to arrive at the claimed invention for the reasons set forth next.

Albrecht does not show or suggest that the claimed subtype, IFN-alpha 5, would be suitable for use in treating HCV. Albrecht defines the term "inteferon-alpha" in column 3, lines 53-56 as referring to "a family of highly homologous species-specific proteins that inhibit viral replication and cellular cellular proliferation and modulate immune response", but he does not specify that the claimed subtype, IFN-alpha 5, is included in this family, and he does not teach that all members of the family are useful in treating HCV. Indeed, Albrecht suggests that one has to select "suitable" members from the family (see column 3, line 56 et seq: "Typical *suitable*

alpha interferons include, but are not limited to. . . ."). Albrecht does not show or suggest that IFN-alpha 5 is a suitable member of the family.

This being the case, the cited references could not set forth even a *prima facie* case of obviousness for a number of reasons. For one thing, there would not be a reasonable expectation of success from the references that the claimed subtype, IFN-alpha 5, would be useful in treating HCV. As aforementioned, Albrecht does not suggest that IFN-alpha 5 is suitable for treating HCV, whereas Foster et al show activity of IFN-alpha 5 in an *in vitro* assay with respect to EMC virus only. As noted by the Examiner on page 5 of the Official Action of June 3, 2003, "the artisan would recognize and appreciate that there is often no known correlation between *in vitro* and *in vivo* results, because the artisan recognizes that an *in vitro* assay cannot duplicate the complex conditions of *in vivo* treatment". This is *a fortiori* true where, as here, the *in vitro* assay is performed with respect to a virus, EMC, which is different than the virus, HCV, that is treated by the claimed method.

In addition, it is respectfully submitted that a combination of the cited references, even if proper, would not arrive at the claimed invention. In this respect, the primary reference, Foster et al teach the use of a different subtype of interferon, IFN-alpha 8, from the subtype claimed, IFN-alpha 5. Accordingly, even assuming for the sake of argument that one of skill in the art would have been motivated to combine Foster et al with Albrecht to arrive at a method for treating HCV, the combination would result in the use of IFN-alpha 8 in such method (also with no reasonable

expectation of success).

Even assuming for the sake of argument that the cited references were properly combinable to arrive at the claimed invention and that there were a reasonable expectation of success, it is respectfully submitted that the evidence in the aforementioned declaration would be sufficient to overcome any alleged *prima facie* case of obviousness set forth by the cited references. In this connection, the paper annexed to the declaration presents data which show that IFN-alpha 5 produces stronger activation of cell signaling and more efficient induction of antiviral genes than IFN-alpha 2 in hepatocytic cells. This finding is surprising and unexpected in view of the fact that, as discussed in the paper and as shown in the Albrecht reference, IFN-alpha 2 was viewed as the preferred IFN-alpha and constitutes the basis of the currently used antiviral therapy of chronic viral hepatitis (see paper at Abstract).

In view of the above, it is respectfully submitted that all rejections and objections of record have been overcome and that the application is now in allowable form. An early notice of allowance is earnestly solicited and is believed to be fully warranted.

Respectfully submitted,

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